CLAIMS ART 34 AMDT

1. A production strain of rhPBGD obtained by use of the DNA fragment, EcoR I - Hind III linear fragment as shown in SEQ ID NO 2 to obtain hemC-deletion in the host JM105-H-R6-C by homologous gene replacement and transforming the resulting strain with the expression plasmid pExp1-M2-BB as shown in SEQ ID NO:1 to yield the final production strain PBGD which is free from production of PBGD of non human origin (Accession No 12915).

2. A method for the preparation of rhPBGD by a method comprising

a) introducing, into a suitable vector, a nucleic acid fragment which includes a nucleic acid sequence encoding PBGD;
b) transforming the production strain according to claim 1 with the vector;
c) culturing the transformed host cell under conditions facilitating expression of the nucleic acid sequence;
d) recovering the expression product from the culture.

3. A method according to claim 2 further comprising a fermentation step.

4. A method according to claim 2 or 3 further comprising a purification step.

5. A method according to claim 4 wherein the purification is performed with a His-Tag (rhPBGD-His).

6. A method according to any of claims 2-5, wherein the PBGD is recombinant human PBGD based on any of Seq. ID NO 3 (clone PBGD 1.1) and Seq. ID NO 4 (non-erythro PBGD 1.1.1).

7. An expression plasmid pExp1-M2-BB as shown in Seq. ID NO 1 for use in the expression of rhPBGD in E. coli.

8. A DNA fragment, EcoR I - Hind III linear fragment as shown in Seq. ID NO 2, capable of obtaining hemC-deletion in a host.

ART 34 AMDT

9. A rhPBGD produced by the method of any of claims 2-6 and able to lower the levels of PBG and ALA in mice during an acute attack of porphyria in a transgenic mouse model where the PBGD gene has partially been knocked-out.

10. A rhPBGD having a stability of at least 6 weeks at 20°C, such as for at least 7 weeks, preferably for 8 weeks.

11. A rhPBGD having a stability resulting in a decrease in activity of less that 10% per month, such as less than 5%.